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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,305	12/06/2001	Charles E. Prussak	ST-UCSD3140	1335

7590  
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08/24/2007

EXAMINER
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GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
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1644

MAIL DATE	DELIVERY MODE
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08/24/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/006,305	PRUSSAK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2-4, 8, 11, 12, 14, 16-21, 23-29, 32-41, 43-51 and 62-75 is/are pending in the application.
- 4a) Of the above claim(s) 14, 16-21, 23-26, 43-51 and 62-67 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-4, 8, 11-12, 27-29, 32-41 and 68-75 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 05/21/2007 has been entered.

Applicant's amendment, filed 05/21/2007, has been entered.

Claims 2, 8, 33, 34 and 68 have been amended.

Claims 2-4, 8, 11-12, 14, 16-21, 23-29, 32-41, 43-51 and 62-75 are pending.

Claims 1, 5-7, 9-10, 13, 15, 22, 30-31, 42, 52-61 have been canceled previously.

Applicant's election without traverse of Group I for examination, and the species wherein Domains I, II and III are fragments of CD154 (i.e. CD40L), while Domain IV comprised a fragment of human TNF $\alpha$  has been acknowledged.

As indicated previously,

for examination purposes, the elected claims 2-4, 8, 11-12, 27-29, 32-41 and 68-75 are being examined to the extent they read on the elected species wherein Domains I, II and III are fragments of CD154 (i.e. CD40L), while Domain IV comprised a fragment of human TNF $\alpha$ .

Claims 14, 16-21, 23-26, 43-51 and 62-67 have been withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to the nonelected inventions and/or species.

2. This Action will be in response to applicant's arguments, filed 05/21/2007.

The rejections of record can be found in the previous Office Actions, mailed 8/1/06 and 01/03/2007.

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3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 2-4, 8, 11-12, 27-29, 32-41 and 68-75 are rejected under 35 U.S.C. § 102(a) as being anticipated by Cantwell et al. (Blood 11 (Part 1): page 423a, November 16, 2001 (see Abstract)).

Cantwell et al. teach generating chimeric TNF genes encoding the receptor-binding domain of TNF lacking the known site(s) for cleavage by matrix metalloproteinase spliced onto transmembrane domains of other members of the TNF family, including CD154 (i.e., CD40 ligand, CD40L) as well as generating recombinant adenovirus vectors encoding these recombinant TNF genes (see Ad-CD154-TNF) as well as transduced cells comprising said nucleic acids and vectors

Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons.

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Although the reference does not disclose all of the claimed characteristics (e.g., SEQ ID NOS., Domains) of the claimed nucleic acids molecules,

given the structural and functional properties of the prior art chimeric TNF-CD154 molecules, including encoding nucleic acids of said constructs; the claimed structural and functional limitations would be inherent properties of the referenced nucleic acid molecules encoding said constructs, including the referenced Ad-CD154-TNF.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. Also, the Courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property.

See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency.

Also, it is noted that the co-inventors of the instant application are co-authors on this Abstract and would have knowledge of the applicability of the prior art teaching to the instant claims.

6. Claims 2-4, 8, 11-12; 27-29, 32-41 and 68-75 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kipps et al. (U.S. Patent No. 7,070,771) AND/OR Kipps et al. (WO 98/26061) in view of Mueller et al. (J. Biol. Chem. 274: 1999) (1449) and newly added Kornbluth (US 2005/0158831 A1) essentially for the reasons of record.

Applicant's arguments in conjunction with the Foon Declaration, filed 05/21/2007, as well as with the Prussak 132 Declaration, filed 10/05/2006, have been fully considered but have not been convincing essentially for the reasons of record.

In particular, applicant submits that the claimed molecules represent a particular combination of elements that one would not readily select from the range of variables suggested by the cited art and that the particular selection claimed, which resulted in near elimination, not just reduction, of soluble TNF $\alpha$  release could not have been predicted.

Further, applicant submits that Mueller et al. only suggests that removal of the disclosed portion of Domain III of the TNF $\alpha$  molecule will reduce release of soluble TNF $\alpha$  in certain cell types;

while evidence has been provided that the particular selection claimed resulted in near elimination, not just reduction of soluble TNF $\alpha$  release (see Foon Declaration).

Applicant further relies upon KSR Int'l Co. v. Teleflex, Inc., 550 US \_\_\_, 2007 WL 123837, at 12 (2007), for the position that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." (emphasis added).

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Here, applicant submits that one could construct a wide range of different constructs following Kipps et al. (to obtain expression in expression-incompetent cell types), and might try to modify cleavage sites in the chimera (to enhance stability). If one did so, one might possibly hope that release of soluble TNFa could be reduced from molecules lacking a cleavage site from Domain III of the TNFa molecule and/or that the chimera might be expressible in otherwise expression-incompetent cell

As discussed during the interview, the cited references would not readily lead one of ordinary skill in the art to predict that soluble TNFa release could be eliminated from cells transfected with the claimed chimera in particular.

In corroboration of that conclusion applicant submits the Foon Declaration, which concludes:

Nothing in the references points one to select a CD154/TNFa chimera lacking a metalloproteinase site in particular, nor do the references offer a reasonable basis upon which to expect that cleavage from such a chimera would be abrogated to the same or greater degree than demonstrated by Mueller, et al. for the TNF molecule they tested. Even in view of the Kipps application's disclosure, one could not have predicted, a priori, the best combination of TNF family member segments to fuse to the domain IV of TNF to create a stabilized molecule.

See paragraph seven (7) of the Foon Declaration.

However, it is also noted that paragraph five (5) of the Foon Declaration acknowledges that Mueller did investigate the in vitro and in vivo biological activity of a "non-cleavable" transmembrane form of mouse TNF and did delete all the known cleavage sites from the murine molecule. Further, the Foon Declaration acknowledges that Mueller demonstrated that this functional TNF molecule was expressed for the most part in a membrane stabilized manner.

While applicant relies, in part, upon the Foon Declaration indication that the relative cleavage of the soluble TNF molecule was cell line dependent, the claims are not limited to any particular cell line.

Therefore, applicant's arguments of unexpected results do not appear to be commensurate in scope with the claims, particularly in view of the motivation and expectation of success in constructing such chimeric TNF-CD40L molecules at the time the invention was made.

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In addition and in response, in part, to paragraph six (6) of the Foon Declaration concerning that "nothing in the Mueller paper would cause one to suspect that removing a metalloproteinase cleavage site from the CD154 element of a TNF $\alpha$  chimera would produce even the same resistance to cleavage enjoyed by the TNF molecule tested by Mueller, the following is noted.

Kornbluth has been added to provide further motivation and expectation of success in modifying the proteinase cleavage site(s) in constructs comprising CD40L as well as TNF by teaching that CD40L containing protease-susceptible amino acid sequences, which can be eliminated by mutagenesis to retard the cleavage of CD40L from fusion proteins, which, in turn, would favor the local persistence of the CD40L stimulus (See entire document, particularly the Discussion of Example on pages 9-10 and paragraphs [0098] – [0099] ).

Also, with respect to the teachings of Kornbluth, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., In re Kahn, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) and In re Dillon, 16 USPQ2d 1897 (Fed. Cir. 1990), *cert. denied*, 500 U.S. 904 (1991).

Here, generating chimeric molecules comprising CD40L and TNF was a simple modification of the cleavage site(s) from either the CD40L or TNF molecules or encoding molecules, wherein the prior art recognized the advantages of such modifications to increase the biological activity or the efficacy of the CD40L and TNF molecules.

With respect to motivation, expectation of success and predictability and the other rationales offered by the Supreme Court, the prior art modified CD40L and TNF molecules, including their integration into chimeric molecules for the very reasons as applicant to generate or derive chimeric molecules comprising CD40L and TNF without cleavage sites that would limit the effects of the chimeric molecule and, in turn, would have been expected to translate into the increased desired biological activity or efficacy of said molecules

In this regard, applicant's reliance on the asserted unpredictability that the particular claimed constructs does not detract from the clear teachings, motivation, expectation of success, predictability, design choices and market forces at the time the invention was made to address the nature of the problems associated with cleavage sites in CD40L and TNF by modifying said cleavage site(s) that limit the efficacy or desired biological activity of said molecules.

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Although it is recognized that there may be some degree of unpredictability at the time the invention was made concerning the ability or the extent of the stability of stabilizing CD40L-TNF on different cell types,

the possibility or even observations of such does not compel a conclusion of non-obviousness herein.

Consistent with KSR, the operative question in this "functional approach" is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions."

The claim is to a structure already known in the prior art that is altered by the mere substitution of one known element for another element known in the field for the same function. The facts themselves show that there is no difference between the claimed subject matter and the prior art but for the combination itself. "[T]he mere existence of differences between the prior art and an invention does not establish the invention's nonobviousness. The gap between the prior art and respondent's system is simply not so great as to render the system nonobvious to one reasonably skilled in the art."

Dann v. Johnston, 425 U.S. 219, 230, 189 USPQ 257, 261 (1976)

The following of record with the addition of Kornbluth et al. addressed above is reiterated for applicant's convenience

Applicant's arguments, in conjunction with the Prussak 132 Declaration have been fully considered but have not been convincing essentially for the reasons of record.

In response to applicant's arguments that there is no or insufficient suggestion to combine the references to modify the prior art to render applicant's invention obviousness, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

While applicant in conjunction with the Prussak Declaration appear to focus on the lack of sufficient motivation and expectation of success on the modifications suggested by Mueller et al. (J. Biol. Chem.274: 1999).

it appears that such assertions appear to overstate the deficiencies of the prior teachings of Mueller et al., and more in particular, the teachings of the combined references.



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In this case the teachings of the prior art references pertaining to the difficulties in preventing the deleterious effects of cleaved TNF $\alpha$  and, in turn, their teachings indicating success in generating chimeric accessory molecules to solve the same or similar problem would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

As pointed out previously, both Kipps et al. (U.S. Patent No. 7,070,771 and WO 98/26061) (see entire documents) teach chimeric molecules, including nucleic acids encoding accessory molecules ligands (and associated vectors, including viral vectors and regulatory regions host cells such as tumor cells and antigen presenting cells and methods of producing the chimeric molecules) which are made up of various domains and sub-domains of molecules derived from the tumor necrosis factor molecules, which, in turn, contain unique properties which lead to the stabilization of their activities and greater usefulness in the treatment of diseases (see entire document, including Abstracts and Summary of the Inventions). The Detailed Description of the Invention these prior art references describe the very CD154 / CD40L domain structures to be utilized as well as TNF $\alpha$  itself as well as the Domain Structure of Tumor Necrosis Factor Family Molecules (e.g. see Table 1 on column 15 of U.S. Patent No. 7,070,771 and page 29 of WO 98/26061).

While the prior art Kipps et al. references contemplate chimeric accessory molecules comprising any domain, sub-domain and portions of the disclosed molecules, including CD154/CD40L and TNF $\alpha$  (e.g., see Detailed Description of the Inventions), these references do not set out the particular nucleic acid molecules comprising a Domain IV fragment of TNF $\alpha$  and the rest of the molecule comprising CD40L per se.

Also, as noted previously, these Kipps et al. references do note that the fourth domain (Domain IV) of the accessory molecule ligand gene(s) is called the distal extracellular domain and that the secondary structures of the accessory molecule(s) were deduced based upon CD40L and human TNF (e.g. see column 14-15, overlapping paragraph of U.S. Patent No. 7,070,771 and pages 27-28 of WO 98/26061).

Further, the disclosures of the co-inventors own prior art references are very similar if not the same as the instant disclosure of generating chimeric accessory molecules comprising any domain, sub-domain and portions of the disclosed molecules, including CD154/CD40L and TNF $\alpha$  (e.g., see Detailed Description of the Inventions) as the instant disclosure.

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While applicant and the Prussak Declaration acknowledge the teachings of Mueller et al., applicant submits that this reference only teaches modifying the wild-type TNF $\alpha$  in certain respects, including that the deletion of the cleavage site alone as not being sufficient to substantially eliminate soluble TNF release.

However, such a limited reading of Mueller et al. itself is not readily apparent and not found convincing with respect to the principles as well as advantages and expected beneficial results that would have been produced by their combination.

Again, the prior art is the same or nearly the same as the instant disclosure with respect to generating the same types of chimeric accessory molecules with the same direction to combining different elements of CD154/CD40L and TNF $\alpha$  to achieve the same or similar advantages and benefits as applicant's disclosure as filed.

As noted previously, Mueller et al. teach the advantages and, in turn, constructs comprising transmembrane TNF $\alpha$ , which include deleting proteolytic cleavage sites of TNF $\alpha$  to prevent the deleterious effects of cleaved TNF $\alpha$  (see entire document, including Abstract, Introduction and Discussion). Mueller et al. also discusses the role of TNF $\alpha$  in association with CD154 / CD40L as well as the use of transmembrane TNF $\alpha$  therapeutically (see Discussion, including page 38117, columns 1-2).

While Mueller's mutants were not human, the combined teachings including the Kipps' references clearly provided for the use of human constructs, particularly in light of their utilities in the treatment of humans.

As indicated above, Kornbluth has been added to provide further motivation and expectation of success in modifying the proteinase cleavage site(s) in constructs comprising CD40L as well as TNF by teaching that CD40L containing protease-susceptible amino acid sequences, which can be eliminated by mutagenesis to retard the cleavage of CD40L from fusion proteins, which, in turn, would favor the local persistence of the CD40L stimulus (See entire document, particularly the Discussion of Example on pages 9-10 and paragraphs [0098] – [0099] ).

Therefore, it would have been prima obvious to the ordinary artisan at the time the invention was made to construct nucleic acids encoding chimeric accessory molecules, including the construction of TNF $\alpha$  on the extracellular domain with domains of CD154 / CD40L in order to take advantage of the known uses of TNF $\alpha$ , but to avoid the deleterious effects of some or pleiotropic properties of TNF $\alpha$ , such as endotoxic shock, as taught by both Kipps et al. references and Mueller et al. Both Kipps et al. references clearly teach mixing and matching members of the TNF family and rely upon the predicted structures of TNF $\alpha$  and CD154/CD40L per se as a basis for their teachings of constructing chimeric accessory molecules. Nucleic acids comprising SEQ ID NO: 1 would have been an expected or intrinsic property of chimeric molecules comprising human TNF $\alpha$  linked to CD154/CD40L Domains I, II and III.

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One of ordinary skill in the art at the time the invention was made would have been motivated to select an extracellular domain of TNF $\alpha$  with CD154/CD40L domains to achieve the use of TNF $\alpha$  and to avoid the deleterious effects of TNF $\alpha$  by constructing chimeric accessory molecules which contain unique properties which lead to the stabilization of their activities and greater usefulness in the treatment of diseases, as taught by the Kipps et al. references.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One cannot show non-obviousness by merely asserting that the references do not provide the sufficient elements of obviousness or by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Applicant's assertions of unexpected results is acknowledged, however the prior art provided sufficient motivation and expectation of success in constructing chimeric accessory molecules, including the construction of TNF $\alpha$  on the extracellular domain with domains of CD154 / CD40L in order to take advantage of the known uses of TNF $\alpha$ , but to avoid the deleterious effects of some or pleiotropic properties of TNF $\alpha$ , such as endotoxic shock, which in turn, is the same asserted advantages relied upon by applicant in the current application. Therefore, the asserted advantages and unexpected results appear to the same or nearly the same as the instant application.

Applicant's arguments have not been found persuasive.

7. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornam, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

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Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 2-4, 8, 11-12, 27-29, 32-41 and 68-75 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 33, 40-50, 60-74 of USSN 10/154,759 and over claims 1, 16-30 and 37-39 of USSN 11/015,117.

Although the claims are not exactly the same, the instant and copending claims are drawn to nucleic acid molecules / constructs encoding chimeric CD40-TNF molecules and their corresponding vectors and host cells.

Therefore, the instant claims and copending claims can anticipate or render obvious one another.

However, it is noted that there may be or are differences in the election of species between the copending USSNs or that the claims in the different copending USSNs may involve patentably distinct elements.

Therefore, applicant is invited to clarify the distinction between the copending claims, as the claims differ in their recitation of sequences or TNF family ligands.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.  
Primary Examiner  
Technology Center 1600  
August 20, 2007

